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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/908,975	07/20/2001	Avi Shoshan	25574	6858

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/908,975	SHOSHAN et al.
Examiner	**Art Unit**
Cynthia B Wilder	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 11, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above, claim(s) *3, 4, 16-28, 31, 32, and 44-60* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 5-15, 29, 30, and 33-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This application has been transferred from Examiner David Gunter in Art Unit 1634 to Examiner Cynthia Wilder in Art Unit 1637. All further correspondence should be directed to Examiner Cynthia Wilder whose contact information appears at the end of the Office Action.

Election/Restriction

2. Applicant's election of Group I, claims 1-15 and 29-43 and species election of human as the organism, cancer as the pathologic state and adult as the stage of development in Paper No. 9 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The claims readable on the elected species are claim 1, 2, 5-15, 29-30 and 33-43. Accordingly, claims 3, 4,16-28, 31, 32 and 44-60 have been withdrawn from consideration as being drawn to a non-elected invention.

Priority

3. Acknowledgment is made of Applicant's claim for domestic priority under 35 U.S.C. 119(e).

Specification

4. The disclosure is objected to because of the following informalities:

5.(a) The priority information recited on the first page of the specification is not recited in the first sentence of the specification (see 37 CFR 1.78(a) and MPEP 201.11). It is suggested amending the disclosure by reciting the priority information in the first sentence of the specification.

(b) At page 14 of the specification, line 19, the disclosure refers to a "Fig. 4." However, no figure 4 was submitted in the instant application. Only three figures were submitted as indicated by the Patent Application Transmittal sheet and specification at page 12 under the "Brief Description of the Drawings". Appropriate correction is required.

(c) At page 14 of the specification, line 7, the word "complimentary" is misspelled in the context of the sentence. It is suggested changing "complimentary" to --complementary--.

(d) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 15. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Applicant should remove or amend the hyperlink(s) such that they no longer "work" in a browser environment as set forth in MPEP 608.01. Appropriate correction is required.

Claim Rejections - 35 USC § 112 Second paragraph: Indefiniteness

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

7. Claims 1, 2, 5-10, 29, 30, 33-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 1, 2, 5-10, 29, 30, 33-39 are vague and indefinite at the recitation of " populate a transcriptome" or "populate a sub transcriptome" because it cannot be determined what is meant by "populate" in relations to the messenger RNAs and transcriptome or sub transcriptome. Likewise a definition of the term has not been described in the specification or claims. Thus a clear meaning of the terminology cannot be ascertained. Clarification is required as to what is encompassed by the terminology in the context of the claim language.

(b) Claims 1, 2, 5-10, 29, 30, 33-39 are vague and indefinite at the recitation of " populate a genome" or "populate a sub genome" because it cannot be determined what is meant by "populate" in relations to the transcription unit and genome or sub genome. Likewise a definition of the term has not been described in the specification or claims. Thus a clear meaning of the terminology cannot be ascertained. Clarification is required as to what is encompassed by the terminology in the context of the claim language.

(b) Claims 1, 2, 5-10, 29, 30, 33-39 are vague and indefinite at the recitation of "capable of hybridizing selectively" because it cannot be determined if "capable of" is a property of the oligonucleotides or a separate step. Additionally, no hybridization conditions for the oligonucleotides have been defined in the specification or claims. Thus, it cannot be determined what conditions are required for the oligonucleotides to selectively hybridize to a set or subset of mRNAs.

Claim Rejections - 35 USC § 102(b)

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 5-15, 29, 30, 33-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Vogelstein et al. (WO 98/53319, November 26 1998). The claims are broadly drawn to an oligonucleotide library for detecting mRNAs that populate a transcriptome or sub transcriptome, wherein the transcriptome or sub transcriptome comprises mRNAs transcribed from a multiplicity of transcription units that populate a genome or sub genome, wherein each oligonucleotide in the plurality is capable of hybridizing selectively to one or a set or subset of mRNAs transcribed from a given transcription unit of the genome or sub genome, wherein at least one transcription unit of the genome encodes one or more mRNA splice variants. The claims further encompass wherein the transcriptome or sub transcriptome is a human and wherein the library of oligonucleotides or a subset thereof is immobilized on a microarray.

Note* *-Transcriptome is defined as all mRNAs transcribed from a transcription unit (hence "RNA transcripts" or "transcripts") in a genome. -Transcription unit is defined as genes (spec., page 2). -Sub transcriptome is defined as a portion of a transcriptome that bears certain biological origin, structure, or function traits, e.g., tissue specificity, disease specificity, developmental specificity, etc (spec., page 5).*

Regarding claims 1, 2, 5-15, 29, 30, 33-43, Vogelstein et al. teach an oligonucleotide library comprising a plurality of oligonucleotides, wherein each oligonucleotide in the plurality is capable of specifically hybridizing to sets of messenger RNAs transcribed from a multiplicity of genes (abstract, col. 13, lines 10-25, page 16, lines 11-18). Vogelstein et al. further teach wherein the transcripts are derived from a human of a normal and pathological tissue sample wherein the pathological condition is cancer (page 91, lines 25-31 and page 101, lines 9-13). Vogelstein et al. further teach wherein plurality of oligonucleotides are attached to a solid support or an array such as a chip for use in high throughput screening assays for the detecting of expression of genes (col. 16, lines 21-24). Therefore, Vogelstein et al. meets all of the claimed limitations of claims 1, 2, 5-15, 29, 30, 33-43 of the instant invention.

10. Claims 1, 2, 5, 8, 9, 29, 30, 33, 34, 36, 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hardy et al. (EP 0 791 660 A1, Feb. 14, 1997). Regarding claims 1, 2, 5, 8, 9, 29, 30, 33, 34, 36, 37, Hardy et al. teach an oligonucleotide library comprising a plurality oligonucleotides, wherein each of the oligonucleotides is capable of hybridizing to one or a set or subset of mRNAs transcribed from a given transcription unit (gene) of a genome. The reference further teaches wherein one of the transcription unit encodes a splice variant (Abstract and page 4, examples 1 and 3, lines 11-19 and 34-55, especially lines 54-55). Hardy et al. further teach wherein the transcribes are derived from human (page 4, lines 34-35). Therefore, Hardy et al. anticipates the limitations of claims 1, 2, 5, 8, 9, 29, 30, 33, 34, 36 and 37 of the instant invention.

Claim Rejections - 35 USC § 102(a) and (e)

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

12. Claims 1, 2, 5-15, 29, 30, 33-43 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by Lockhart et al. (US 6,040,138, patent publication date: March 21, 2000 for 35 U.S.C. 102(a) rejection and patent filing date: September 15, 1995 for 35 U.S.C. 102(e) rejection). Regarding claims 1, 2, 5-15, 29, 30, 33-43, Lockhart et al. teach a library comprising a plurality of oligonucleotides, wherein each of the oligonucleotides are capable of hybridizing to a set or subset of mRNAs transcribed (transcriptome) from a multiplicity of genes of a genome. Lockhart further teaches wherein the library is spotted on a microarray. (see Abstract and col. 2, lines 56-67 to col. 3, line 1 and col. 21, lines 5-36). Lockhart et al. further teach wherein the transcriptome is human and wherein the transcriptome comprises samples of a pathological

condition, e.g., cancer, pathological tissue or patient suffering from a condition such as e.g., cancer (col. 4, lines 64-67 to col. 5, lines 5 and col. 11, lines 41-52). Therefore, Lockhart et al. meets all of the claimed limitations of claims 1, 2, 5-15, 29, 30, 33-43 of the instant invention.

Claim Rejections - 35 USC § 102(e)

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

14. Claims 1, 2, 5-15, 29, 30, 33-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Schweighoffer et al. (US 6,251,590 B1, filed March 24, 1998). Regarding claims 1, 2, 5-15, 29, 30, 33-43, Schweighoffer et al. teach an oligonucleotide library comprising a plurality of oligonucleotides capable of hybridizing to alternative forms of splicing mRNAs typical of a physiological condition (col. 11, lines 14-16) or pathophysiological state or developmental stage (col. 12, lines 8-11 and col. 17, lines 51-53), said library comprising plurality of cDNAs generally double stranded in nature corresponding to RNA regions specific of alternative splicing (col. 10, lines 12-

18). Schweighoffer et al. teach wherein the transcribed RNAs (transcriptome) are derived from a cell, tissue, an organ or a biopsy, e.g. cancer biopsy of a sample from a human or mammal source (col. 3, lines 1-8). The reference further teach wherein the pathological condition is preferably cancer (col. 14, lines 17-51). Schweighoffer et al. additionally teach wherein the library comprising the plurality of oligonucleotides is capable of being overlaid (spotted or coated) on a solid support, such as a chip or biochip (microarray). Therefore, in view of the foregoing, Schweighoffer et al. meets all of the claimed limitations of 1, 2, 5-15, 29, 30, 33-43 of the instant invention.

15. Claims 1-2, 5-15, 29, 30, 33-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Mack (US 6,303,301 B1, filing date May 29, 1998). Regarding claims 1, 2, 5-15, 29, 30, 33-43, Mack teaches discloses methods of identifying alternatively spliced nucleic acids in a sample, using microarrays of oligonucleotides which are derived from the exons of genes. In columns 11-12, Mack discusses alternative splicing, and notes that "in some embodiments of the invention, alternative splicing are monitored". The reference teaches wherein high density oligonucleotide arrays are designed against specific sequence diversity to detect the level of each of the sequences produced by alternative splicing and adenylation (column 12, lines 18-21, 48-55). Mack teaches that these oligonucleotides are designed to be complementary to particular sub-sequences of the genes whose expression they are to detect. The reference states that thus the oligonucleotides are capable of specifically hybridizing to the target nucleic acid they are to detect (col. 17, lines 9-13). At column 14, Mack discloses that the target nucleic acid sample is total mRNA isolated from a biological

sample such as any biological tissue or fluid or cells from any organism including a human. Mack discloses that the sample may be a clinical sample derived from a patient (col. 14, lines 34-38 and 47-61). Mack discloses wherein the sample may be derived from normal or malignant cells derived from a cancerous tissue (See examples 1 and 2). At column 41, Mack discloses that arrays were generate specifically to identify alternatively spliced forms of targets (col. 41, lines 24-36 and 51-56). The probes were selected such that each exon for a given message (transcribed RNAs or transcriptome) was represented on the array and Mack notes that "In this way, specific loss of signal from a sub set of probes corresponding to a particular exon would indicate a splice variant form (column 41, lines 47-55). As such, Mack meets all of the limitations of the above rejected claims.

Conclusion

16. No claims are allowed.

17. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Veculescu et al. (Nature Genetics, December 1999) discloses analysis of human transcriptomes using serial analysis of 84 libraries.

Contact Information

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Group's receptionist at (703) 308-0196.

cbw
May 1, 2003

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637